PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2006/000273	13.01.2006	14.01.2005

International Patent Classification (IPC) or both national classification and IPC
INV. G01N33/68 G01N33/86

Applicant
ABLYNX N.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	see form PCT/ISA/210	Lunter, P Telephone No. +31 70 340-8908

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	17-18
	No:	Claims	1-16, 19-22
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-22
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

D1 Murdock et al., Thromb Haemost 78, 1272-1277 (1997)
D2 Favaloro et al., Thromb Haemost 84, 541-547 (2000)
D3 Favaloro et al., Am J Clin Path 114, 608-618 (2000)
D4 WO 01/02853
D5 Veyradier et al., Int J Clin Lab Res 28, 201-210 (1998)
D6 Vanhoorelbeke et al., Thromb Haemost 83, 107-113 (2000)
D7 Favaloro et al., Blood Coag Fibrinolysis 2, 285-291 (1991)
D8 Tsai et al., New Eng J Med 339, 1585-1594 (1998)
D9 Lattuada et al., Haematologica 88, 1029-1034 (2003)
D10 WO 2004/062551
D11 WO 00/24781

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The present application does not meet the requirements of Article 33(2) PCT as claims 1-16 and 19-22 are not novel.

2 The subject-matter of independent claim 1 is anticipated by D1-D9, which disclose methods of discriminating between von Willebrand disease (vWD) subtypes (D1-D3, whole documents; D4, page 2-12; D5-D7, whole documents), thrombotic thrombocytopenic purpura (TTP) (D8, whole document) and HELLP syndrome (D9, whole document), by determining the amount of activated von Willebrand Factor (vWF) in a blood sample of patients. Thus, the subject-matter of independent claim 1 is not novel.

3 The subject-matter of independent claim 21 is anticipated by documents D1-D4, D6-7 and D10-D11, which disclose binding agents for activated vWF and kits containing them (D10, page 3, page 7-8; D11, page 2-3). Thus, the subject-matter of independent claim 21 is not novel.

4 The subject-matter of independent claim 22 is anticipated by D1-D3, which disclose the use of antibodies binding to activated vWF for the differentiation of vWD subtypes. Thus, the subject-matter of independent claim 22 is not novel.

5 Even if the objections noted above could be overcome, the present application would not meet the requirements of Article 33(3) PCT as claims 1-22 do not involve an inventive step.

6 Independent claims 1 and 22 recite a method for distinguishing between different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets, and the use of an antibody specifically recognizing activated vWF in such a method, respectively. Independent claim 21 recites a kit for determining vWF amounts.

7 Thus, the problem this application addresses is therefore how to provide an alternative assay to distinguish between different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets. The solution is to use an antibody specifically recognizing active vWF in the presence of inactive vWF.

8 The solution cannot be regarded as inventive as it represents obvious alterations from those in D1-D11 which are well within the knowledge and abilities of the skilled person.

9 Dependent claims 2-20 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to novelty or inventive step as the subject matter of said claims is either disclosed in the cited prior art or also falls within the knowledge and ability of the skilled person (D1-D11).

10 All claims meet the requirement of Article 33(4) PCT as they are industrially applicable.

Re Item VII

Certain defects in the international application

1 Documents D1-D9 and D11 are not mentioned in the description (Rule 5.1(a) (ii) PCT).

2 Independent claims 1, 21 and 22 are not drafted in the two-part form (Rule 6.3. PCT).

Re Item VIII

Certain observations on the international application

1 The present application does not meet the requirements regarding clarity, disclosure and support for the following reasons (Article 5/6 PCT).

2 Independent claims 1 and 22 recite a method and a use of an antibody for distinguishing different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets. The methods are merely exemplified by studies on vWD type 2B, TTP and HELLP syndrome. The skilled person would therefore not be able to find threshold values of activated vWF for other diseases without inventive skill or undue experimentation. Thus, the scope of the claims are broader than is justified by the contribution to the art.

3 Independent claims 1 and 22 lack essential technical features as they do not recite which ranges of activated vWF correlate with the "different states or forms of the disease or disorder".

4 Independent claims 1, 21 and 22 are unclear, as the term "activated vWF" is unclear. vWF has multiple binding affinities towards e.g. platelet gpIb, collagen and Factor VIII. Thus, this term could indicate any of these binding activities of vWF.

5 Independent claim 21 is unclear due to usage of the term "one or more parts, elements or components of kits for binding assays known per se" and the term "...an agent that binding agent...".